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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/670,537	09/27/2000	Andrew P. Mazar	38369-169219	6771

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EXAMINER

JONES, DAMERON LEVEST

ART UNIT	PAPER NUMBER
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1616

DATE MAILED: 11/06/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/670,537

Applicant(s)

MAZAR ET AL.

Examiner

D. L. Jones

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-49 is/are pending in the application.
- 4a) Of the above claim(s) 1-20, 24, 26, 28, 32-34, 37, 40, 42, 44, 46 and 48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-23, 25, 27, 29, 31, 35, 36, 38, 39, 41, 43, 45, 47 and 49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 September 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6. 6) ☐ Other: _____

ACKNOWLEDGMENT

1. The Examiner acknowledges receipt of the following: (a) Paper No. 7, filed 1/17/02, wherein the specification was amended and a sequence listing was submitted. (b) paper No. 10, foiled 8/6/02, wherein Applicant submitted a corrected substitute sequence listing.

Note: Claims 1-49 are pending.

APPLICANT'S INVENTION

2. Applicant's invention is directed to uPA containing compounds and uses thereof.

RESPONSE TO APPLICANT'S ELECTION

3. Applicant's election with traverse of Group III in Paper No. 19, filed 8/20/03, is acknowledged. The traversal is on the ground(s) that while Groups II and III are patentably distinct, a thorough search of the elected claims of Group III will include art relevant to the claims of Group II. Thus, in Applicant's opinion, a search of both groups does not pose a burden to the Examiner. This is found non-persuasive because as stated in the office action mailed 6/18/03, Paper No. 17, and in Applicant's response, the inventions are distinct. Also, note that claim 13 which is the basis of Group II reads on an uPA active site targeting compound while claim 21 that is the basis of Group III reads on an uPA active site targeting peptide compound. Hence, a search of Group II is not the same scope as Group II because Group II encompasses a multitude of compounds. It is noted that only Groups II and III were traversed. Therefore, the

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remaining group (Group I) has been viewed as an election without traverse. Hence, the restriction requirement is still deemed proper and is therefore made FINAL.

Note: Claims 21-23, 25, 27, 29, 31, 35, 36, 38, 39, 41, 43, 45, 47, and 49 are directed to the elected invention. The full scope of Group III has been searched.

WITHDRAWN CLAIMS

4. Claims 1-20, 24, 26, 28, 30, 32-34, 37, 40, 42, 44, 46, and 48 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention/species.

112 REJECTIONS

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22, line 5: The claim as written is ambiguous because it is unclear whether the third formula actually contains a chelator. Specifically, does 'Chelator(empty)' mean that there is no chelator present? If so, Applicant is respectfully requested to delete that portion of the formula since the formula, as written, does not allow a chelator to be present.

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102 REJECTIONS

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 21, 23, 35, and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Higgins et al (Archives of Biochemistry and Biophysics, 1986, Vol. 249, No. 2, pp. 418-426).

Higgins et al disclose the incorporation of a fluorescent probe into active sites of one and two chain tissue type plasminogen activators. Dansyl-glutamyl-glycyl-arginyl chloromethyl ketone with both forms of t-PA. It is anticipated that the fluorescently labeled tissue plasminogen activator (t-PA) is useful in probing the interaction of one and two chain t-PA with other proteins (see entire document, especially, abstract; page 419, column 1, first complete paragraph; page 426, column 1, first complete paragraph).

Hence, both Higgins et al and Applicant disclose an uPA active site targeting peptide compound that bind to one or more exosites of t-PA having a detectable label.

9. Claims 21, 23, 35, 36, 38, 39, 41, and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Ploug et al (Biochemistry, 1998, 37, 3612-3622).

Ploug et al disclose the photoaffinity labeling of the human receptor for urokinase-type plasminogen activator (uPA) using a decapeptide antagonist. UPA is bound to its cellular receptor, uPAR, which renders the cell surface a favored site for

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plasminogen activation. Thus, the peptide antagonist SLNFSQYLWS was rendered photoactive by replacing residues important for uPAR binding with photochemically active derivatives of phenylalanine (see entire document, especially, abstract). The photoaffinity labeling of uPAR involved combining suPAR and equimolar amounts of 125I-labeled photoactive peptide dissolved in phosphate and NaCl (page 3614, column 1, third complete paragraph).

Hence, both Ploug et al and Applicant disclose an uPA active site targeting peptide compound that bind to one or more exosites of a uPAR binding epitope having a detectable label.

10. Claims 21-23, 25, 27, 29, 31, 35, 36, 38, 39, 41, 43, 45, 47, and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Rabbani et al (WO 99/485509)

Rabbani et al disclose urokinase plasminogen activator receptor as a target for diagnosis of metastases in vivo (see entire document, especially, abstract). In a preferred embodiment, metastases in a subject is detected by administering labeled molecules which bind specifically to uPAR (page 6, lines 3-17; page 9, lines 5-12; page 19-20, 'Diagnosis and Imaging of Metastasis'; page 20, lines 24-35; page 32, claim 1). The labeled molecule is labeled anti-uPAR antibody or fragments containing the uPAR binding domain or peptide mimetics of uPAR (page 6, lines 18-24). The peptide mimetics are selected to mimic the following sequences of human uPA:

VPSNCDCLNGGTCVSNKYFSNIHWCNC (Sequence 1) or

DCLNGGTCVSNKYFSNIHWCN (Sequence 2) [page 12, lines 6-14). The invention

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further disclose that various methods can be used to detect the accumulated labeled material in vivo. Possible methods include x-ray, CAT scan, magnetic resonance imaging, sonography, and positron emission tomography (page 9, lines 12-16; page 20, lines 7-22). The peptide mimetic can be detectably labeled using various methods including using enzymes (pages 15-16, bridging paragraph). Possible labels include radioisotopes such as ^{125}I , ^{131}I , or $^{99\text{m}}\text{Tc}$ (page 16, lines 3-10). When the fluorescently labeled peptide is exposed to light of the proper wavelength, its presence may be detected due to fluorescence (page 16, lines 13- page 17, line 6). The modes of administration includes intravenous administration (page 17, lines 34-36).

Hence, both Rabbani et al and Applicant disclose uPA active site targeting peptide compounds having a detectable label or therapeutic moiety and uses thereof.

11. Claims 21- 23, 25, 27, 29, 31, 35, 36, 38, 39, 41, 43, 45, 47, and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Jones et al (WO 98/21230).

Jones et al disclose cyclic peptides that bind to urokinase type plasminogen activator receptors. The peptides have eleven amino acids joined by a linking unit (see entire document, especially, abstract). The peptide compositions may be used for the inhibition of various applications such as proteolysis, programmed gene expression, cell motility, migration, morphogenesis, activation of certain progrowth factors, angiogenesis, tumor metastasis, retinal neovascularization, and tissue remodeling. The peptides may contain a radioactive, fluorogenic, chromogenic, or chemical label and may be used to quantify urokinase type plasminogen activator receptor levels in tissue

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samples or as a diagnostic and prognostic tool in all diseases where the receptor plays a pathological role (page 1, lines 5-22; page 7, line 6 through page 8, line 25; page 22, lines 4-12).

Hence, both Jones et al and Applicant disclose uPA active site targeting peptide compounds having a detectable label or therapeutic moiety and uses thereof.

SPECIFICATION

12. The disclosure is objected to because of the following informalities: Applicant needs to insert the continuing data on the first line of the specification. Specifically, Applicant needs to insert 'This application claims benefit of provisional application 60/157,012, filed 10/01/99'.


Appropriate correction is required.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (703) 308-4640. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (703) 308 - 2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



D. L. Jones
Primary Examiner
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October 30, 2003